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Proceeding Paper

The Reaction of 1,6-Diamino-4-aryl-2-oxo-1,2-dihydropyridine-3,5-Dicarbonitriles with Certain Electrophilic Agents †

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Abstract: The reaction of 1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles, which are easily available through the reaction of cyanoacetohydrazide with arylmethylene malononitriles, with ninhydrin leads to the formation of novel dihydroindeno[1,2-e]pyrido[1,2-b][1,2,4]triazines. Another active carbonyl compound, glyoxal, reacts with 1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles under mild conditions to give functionalized 6-oxo-6H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles.

Keywords: 1,6-diaminopyridines; cyanoacethydrazide; malononitrile; heterocyclization; ninhydrin; glyoxal

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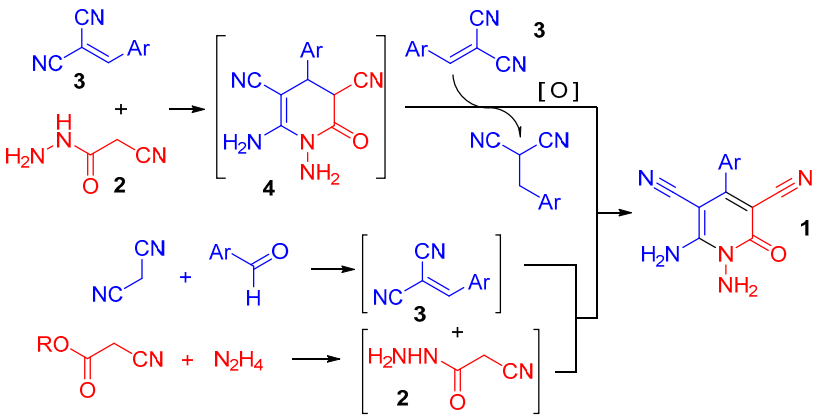
1. Introduction

1,6-Diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles **1** were first prepared by Soto and colleagues in 1981 by treating cyanoacethydrazide **2** with 2 eq. arylmethylene malononitriles **3** in the presence of bases [1] (Scheme 1). The compounds **1** can also be synthesized by ternary cyclocondensation of corresponding aromatic aldehydes with malononitrile and hydrazide **2** generated in situ. The title compounds **1** are highly functionalized pyridine derivatives and are promising reagents useful for the preparation of nitrogen-bridged polyheterocyclic ensembles [2]. However, despite the presence of neighboring active amino groups, there are only a few reports on the reactions of 1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles with electrophilic agents such as active carbonyls [2]. Hence, we decided to fill this gap by performing reactions of the title compounds with ninhydrin and glyoxal.

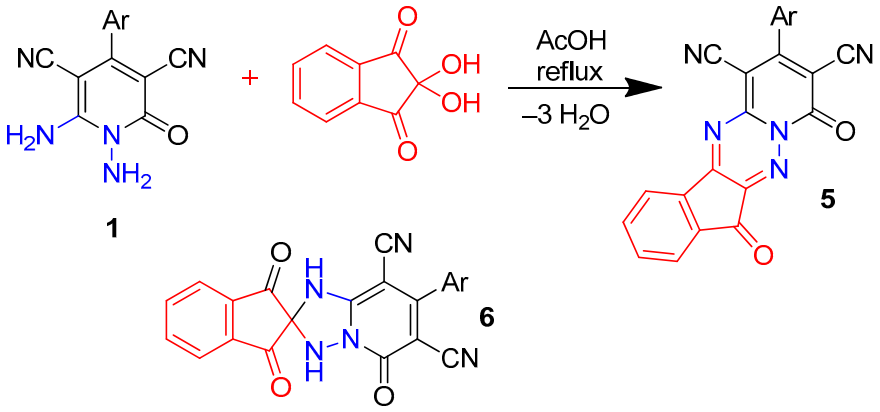


Scheme 1. Preparation of 1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles **1**.

2. Results and Discussion

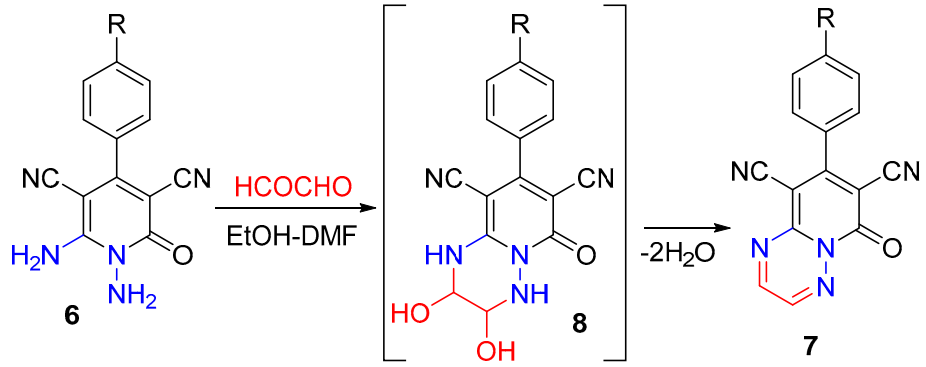
First, we prepared 1,6-diamino-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles **1** according to the reported procedure [1]. As reported in the original paper of Soto and colleagues [1], pyridine-3,5-dicarbonitriles **1** can be isolated in high yields only when arylmethylene malononitriles **3** are taken in two-fold excess with respect to the starting hydrazide **2**. So, the true oxidant needed to oxidize intermediate tetrahydropyridine species **4** (Scheme 1) is arylmethylene malononitrile **3**, not air oxygen.

We found that, upon treatment of 1,6-diamino-2-oxo-1,2-dihydropyridine- 3,5-dicarbonitriles **1** with ninhydrin in boiling acetic acid, dihydroindeno[1,2-e]pyrido[1,2-b][1,2,4] triazines **5** were isolated in good yields (Scheme 2). The formation of spiro compounds **6** was not confirmed in the reaction.



Scheme 2. The preparation of dihydroindeno[1,2-e]pyrido[1,2-b][1,2,4]triazines **5**.

When compounds **1** were treated with a small excess of aqueous glyoxal, 8-aryl-6-oxo-6H-pyrido[1,2-b][1,2,4]triazine-7,9-dicarbonitriles **7** were isolated as deep green colored solids easily soluble in common organic solvents such as EtOAc or acetone. The compounds **7** are examples of the poorly studied heterocyclic system of pyrido[1,2-b][1,2,4]triazine. Obviously, the reaction proceeds through the formation of the corresponding semi-aminals **8** with subsequent dehydration (Scheme 3).



Scheme 3. The preparation of pyrido[1,2-b][1,2,4]triazines **7** (R = Hal, MeO).

3. Experiments

Preparation of Dihydroindeno[1,2-e]pyrido[1,2-b][1,2,4]triazines **5**

A mixture of pyridines **1** (0.01 mol) and ninhydrin (0.01 mol) was dissolved in a small amount of AcOH (1–2 mL) and then was heated under reflux. The reaction was monitored by TLC (eluent—EtOAc or acetone, Sorbfil-A plates). After complete consumption of **1**, the reaction mixture was allowed to cool and left to stand overnight. The brick-red solid was filtered off and washed with EtOH to give pure dihydroindeno[1,2-e]pyrido[1,2-b][1,2,4]triazines **5**.

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